

IN THE SPECIFICATION

Page 8, line 1, to page 10, line 17, please amend as follows:

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 is a diagram illustrating components of healthy nucleus pulposus tissue in a vertebrate. Figure 1A is a magnified proteoglycan aggregate.

Figure 2 is a diagram illustrating a process for preparation and use of a cross-linked matrix of porcine nucleus pulposus tissue in a preferred embodiment of the invention.

Figure 3 is a photographic reproduction of an SDS-PAGE (sodium dodecyl sulfate polyacrylamide gel electrophoresis) analysis comparing the amount of proteins extracted from a cross-linked matrix of the present invention with a non-cross-linked control. Lane A shows non-cross-linked control shows substantial protein extraction, and Lane B shows cross-linked matrix demonstrates reduced protein extraction.

Figure 4 is a photographic comparison of an H & E (hematoxylin and eosin) stained section of fresh porcine nucleus pulposus tissue with a cross-linked matrix of the present invention, both at 300X magnification. The fresh nucleus pulposus shows round, nucleated chondrocytes and intact pericellular matrix “nests,” while the cross-linked matrix shows disrupted, crenated cell fragments, minimal cell membrane material, and further isopropanol sterilization.

Figure 5 is a photographic reproduction of a stained nitrocellulose membrane comparing the reactivity of Type II collagen digested from a cross-linked matrix of the present invention and a non cross-linked control. Lane A shows pepsin digests of non-cross-linked control react with Type II collagen antibodies. Lane B shows pepsin digests of cross-linked matrix does not react with Type II collagen antibodies.

Figure 6 is a comparison graph of the hydraulic/swelling capacity of a cross-linked matrix of the present invention and a non-cross-linked control. The cross-linked matrix retains 95% hydraulic capacity.

Figure 7 is a diagram of an experimental process used to demonstrate stimulation of sheep cell ingrowth, proliferation, and new matrix synthesis in an embodiment of the present invention comprising a cross-linked matrix combined with bone protein growth factors (BP).

Figure 8 ~~is a graph and a photograph indicating~~ shows the growth factor stimulation of matrix synthesis. The graph shows the results of an Alcian blue assay for matrix production in sheep nucleus pulposus cells stimulated by growth factors. Significant stimulation of matrix production occurred only at μ g BP concentrations.

Figure 9 is a graph indicating the results of immunogenicity tests for a cross-linked matrix of the present invention in rabbit immunizations and sheep serum. Low antibody titers to cross-linked matrix in rabbit immunizations. There were no serum antibodies to cross-linked matrix *in vivo* (first sheep).

Figure 10 is a diagram of the protocol for an *in vivo* study of a matrix and growth factor combination of the present invention.

Figure 11 is a radiograph of a vertebral column from a sheep sacrificed at 2 months after an injection of a matrix and growth factor combination in an *in vivo* study of an embodiment of the present invention. Treated and control discs were of normal size and the disc structures appeared normal. The untreated discs showed disjunct endplates, bone resorption and remodeling.

Figure 12A, Figure 12B and Figure 12C ~~is a~~ are photographic reproductions of histology slides of vertebral discs of a sheep sacrificed at 2 months after an injection of a matrix and

growth factor combination of the present invention. Figure 12A shows untreated disc, Figure 12BB shows control, and Figure 12C shows treated disc. After two months post-infection, the untreated disc exhibits extensive degeneration, while the cross-linked matrix/BP treated disc retains normal structures similar to control disc.

Figure 13 is a radiograph of a vertebral column of a sheep sacrificed at 4 months after an injection of a matrix and growth factor combination in an *in vivo* study of the present invention. There were no apparent radiographic differences between discs in 4-month sheep.

Figure 14 is a photographic reproduction of histology slides of vertebral discs of a sheep sacrificed at 4 months after an injection of a matrix and growth factor combination of the present invention. Four months post-injection, untreated disc exhibits degenerative changes, while cross-linked matrix/BP-treated disc is similar to control disc: normal gelatinous nucleus, regular annulus and intact endplates.

Figure 15A and Figure 15B ~~is a~~ are graphs representing the results of an ELISA performed to measure the synthesis of Type II collagen and Chondroitin-6-sulfate under growth factor stimulation.

Figure 16aA ~~is a graph~~ and Figure 16B show growth factor stimulation of proteoglycan synthesis in human intervertebral disc nucleus pulposus cells. Shown are graphs (Figure 16A, 8 day incubation; Figure 16B, 9 day incubation) indicating the results of an Alcian blue assay for proteoglycan synthesis in human intervertebral disc cells stimulated by growth factor.

~~Figure 16b is a graph indicating the results of an Alcian blue assay for proteoglycan synthesis in another human intervertebral disc cells stimulated by growth factor.~~

Figure 17 shows growth factor stimulation of proteoglycan synthesis in baboon intervertebral disc nucleus pulposus cells. Shown is a graph depicting the results of an Alcian

blue assay for proteoglycan synthesis in baboon intervertebral disc cells stimulated by growth factor.

Figure 18 is an SDS-PAGE gel of HPLC fractions 27-16 from a sample of BP.

Figure 19 is an SDS-PAGE gel of HPLC fractions 27-16 with identified bands indicated according to the legend of Figure 20.

Figure 20 is an SDS-PAGE gel of BP with identified bands indicated.

Figure 21 is a 2-D (two-dimensional) SDS-PAGE gel with internal standards indicated by arrows.

Figure 22 is a 2-D SDS-PAGE gel with circled proteins (growth factors) identified as in legend.

Figures 23A-23O are Mass Spectrometer results for tryptic fragments.

Figure 24 is a 2-D gel Western blot with anti-phosphotyrosine antibody.

Figures 25A-25D are 2-D gel Western blots with antibodies for the indicated proteins. For Figure 25A, the growth factors are BMP-3 and BMP-2; for Figure 25B the growth factors are BMP-3 and BMP-7; for Figure 25C the growth factors are BMP-7 and BMP-2; and for Figure 25D the growth factors are BMP-3 and TGF- β 1.

Figure 26 is a PAS (periodic acid schiff) stained SDS-PAGE gel of HPLC fractions.

Figure 27 is an anti-BMP-7 stained SDS-PAGE gel of PNGase F treated BP.

Figure 28 is an anti-BMP-2 stained SDS-PAGE gel of PNGase F treated BP.

Figures 29A-29B are bar charts showing explant mass of glycosylated BP samples (Figure 29A) and ALP Score (Figure 29B) of the same samples.

~~Figure 30 is a chart showing antibody listing and reactivity.~~

~~Figures 31A-31B together comprise a chart showing tryptic fragment sequencing data.~~

~~Figures 32A-32F together comprise a chart showing tryptic fragment mass spectrometry data.~~

Figures ~~33A-33B~~ 30A-30B are an SDS-gel of BP (Figure ~~33B~~30B) and a scanning densitometer scan (Figure ~~33A~~30A).

~~Figure 34 is a chart illustrating the relative mass of major components of BP.~~

Page 30, lines 6-10, please amend as follows:

An SDS-PAGE gel of BP was also analyzed by Western immunoblot with a series of antibodies, as listed in ~~Figure 30~~ Table 1. Visualization of antibody reactivity was by horse radish peroxidase conjugated to a second antibody and using a chemiluminescent substrate. The reactivities are as indicated in ~~Figure 30~~ Table 1.

Page 30, please insert the following after line 9:

TABLE 1 – ANTIBODY INFORMATION

Specificity	Antigen	Host Species	PC/MC	Source	Catalog No.
TGF- β 1 (human)	Protein	Rabbit	Polyclonal	Promega	G1221
TGF- β 2 (human)	Peptide	Rabbit	Polyclonal	Santa Cruz Biotechnology	sc-90
TGF- β 3 (human)	Peptide	Rabbit	Polyclonal	Santa Cruz Biotechnology	sc-82
BMP-2 (human)	Protein	Rabbit	Polyclonal	Austral Biologics	PA-513-9
BMP-3	Peptide	Chicken	Polyclonal	Research Genetics	NA

TABLE 1 – ANTIBODY INFORMATION

Specificity	Antigen	Host Species	PC/MC	Source	Catalog No.
(human)					
BMP-4 (human)	Peptide	Goat	Polyclonal	Santa Cruz Biotechnology	sc-6896
BMP-5 (human)	Peptide	Goat	Polyclonal	Santa Cruz Biotechnology	sc-7405
BMP-6 (human)	Peptide	Mouse	Monoclonal	Novocastra Laboratories	NCL-BMP6
BMP-7 (human)	Peptide	Rabbit	Polyclonal	Research Genetics	NA
FGF-1 (human)	Peptide	Goat	Polyclonal	Santa Cruz Biotechnology	sc-1884
osteonectin (bovine)	Protein	Mouse	Monoclonal	DSHB	AON-1
osteocalcin (bovine)	Protein	Rabbit	Polyclonal	Accurate Chemicals	A761/R1H
serum albumin (bovine)	Protein	Rabbit	Polyclonal	Chemicon International	AB870
transferrin (human)	Protein	Chicken	Polyclonal	Chemicon International	AB797
apo-A1 lipoprotein (human)	Protein	Goat	Polyclonal	Chemicon International	AB740

Page 30, lines 22-31, please amend as follows:

The various components of the BP were characterized by mass spectrometry and amino acid sequencing of tryptic fragments where there were sufficient levels of protein for analysis. The major bands in the 1-D (one dimensional) gels were excised, eluted, subjected to tryptic

digestion, purified by HPLC and sequenced by methods known in the art. The major bands are identified by band number, as shown in Figures 19 and 20. The sequence data was compared against known sequences, and the fragments are identified as shown in ~~Figure 31~~ Table 2. In some cases, the identification is tentative due to possible variation between the human and bovine sequences and/or possible post translational modifications, as discussed below.

Page 30, please insert the following Table after line 31:

TABLE 2
IDENTIFICATION OF PROTEINS BY AMINO ACID SEQUENCING OF TRYPTIC FRAGMENTS

Band	Sample	Sequence Data	Best Database Match	Match	Identification	Species	Acc. No.	AAs
1								
2	fx 49 (1579)	XLAAAGYDVEK (SEQ ID NO:1)	ALAAAGYDVEK (SEQ ID NO:2)	11/11	Histone H1.c	Human	87668 (NCBI)	65-75
3	fx 67 (1346)	SLEKVCADLIR (SEQ ID NO:3)	SLEKVCADLIR (SEQ ID NO:3)	11/11	40s Ribosomal Protein S20	Rat	R3RT20 (PIR)	31-41
4	fx 65	VVCGMLGFPSEAPV (SEQ ID NO:4)	VVCGMLGFPGEKRV (SEQ ID NO:5)	11/14	LORP	Mouse	AAC95338	213-226
5	N terminal seq	STGVLLPLQNNELPG (SEQ ID NO:6)	STGVLLPLQNNELPG (SEQ ID NO:6)	15/15	BMP-3	Human	4557371 (NCBI)	290-304
	fx 72 (3925)	STGVLLPLQNNELPGA EYGY (SEQ ID NO:7)	STGVLLPLQNNELPGA EYQY (SEQ ID NO:7)	20/20	BMP-3	Human	4557371 (NCBI)	290-309
	fx 74 (3409)	STGVLLPLQ (SEQ ID NO:8)	STGVLLPLQ (SEQ ID NO:8)	9/9	BMP-3	Human	4557371 (NCBI)	290-298
6	fx 55 (1566)	SQTLQFXE (SEQ ID NO:9)	SQTLQFDE (SEQ ID NO:10)	7/8	BMP-3	Human	4557371 (NCBI)	346-353
	fx 47	VYAF (SEQ ID NO:11)	No match		???			
	N terminal seq	HAGKYSREKNTAP (SEQ ID NO:12)	HGGKYSREKNQPKP (SEQ ID NO:13)	11/14	α 2-Macroglobulin Receptor Assoc. Pro.	Human	P30533 (Swiss-Prot)	31-46
	fx 57 (1438)	SQTLQFDEQ (SEQ ID NO: 14)	SQTLQFDEQ (SEQ ID NO:14)	9/9	BMP-3	Human	4557371 (NCBI)	346-354
	fx 57 (1652)	SLKPSNHA (SEQ ID NO:15)	SLKPSNHA (SEQ ID NO:15)	8/8	BMP-3	Human	4557371 (NCBI)	410-417
7	fx 51 (1093)	AALRPLVKP (SEQ ID NO:16)	AALRPLVKP (SEQ ID NO:16)	9/9	60s Ribosomal Protein L32	Mouse	P17932 (Swiss-Prot)	1-9
	fx 37 (no MS)	AHIQVERYV (SEQ ID NO:17)	AIVER (SEQ ID NO:18)	5/5	60s Ribosomal Protein L32	Mouse	P17932 (Swiss-Prot)	109-113

TABLE 2
IDENTIFICATION OF PROTEINS BY AMINO ACID SEQUENCING OF TRYPTIC FRAGMENTS

Band	Sample	Sequence Data	Best Database Match	Match	Identification	Species	Acc. No.	AAs
	fx 37 (no MS)	AHIQVERYV (SEQ ID NO:17)	HQSDRYV (SEQ ID NO:19)	5/7	60s Ribosomal Protein L32	Mouse	P17932 (Swiss-Prot)	22-28
8	fx 78	XALFGAQLGXALGPI (SEQ ID NO:20)	No match		???			
9	fx 56 (1567)	SQTLQFDEQT (SEQ ID NO:21)	SQTLQFDEQT (SEQ ID NO:21)	10/10	BMP-3	Human	P12645 (Swiss-Prot)	346-355
11	fx 55 (1311)	SQTLXF (SEQ ID NO:22)	SQTLQF (SEQ ID NO:23)	5/6	BMP-3	Human	4557371 (NCBI)	346-351
	fx 47 (1772)	VLATVTKPVGGDK (SEQ ID NO:24)	VLATVTKPVGGDK (SEQ ID NO:24)	13/13	60s Ribosomal Protein L6	Human	Q02878 (Swiss-Prot)	87-99
	fx 76 (1795)	XVFAL (SEQ ID NO:25)	VFAL (SEQ ID NO:26)	4/4	60s Ribosomal Protein L6	Human	Q02878 (Swiss-Prot)	273-276
	fx 61 (1145)	AVPQLQGYLR (SEQ ID NO:27)	APQLQGYLR (SEQ ID NO:28)	9/10	60s Ribosomal Protein L6	Human	Q02878 (Swiss-Prot)	262-271
18								
22	fx 58 (1101)	ALDAAAYCFR (SEQ ID NO:29)	ALDAAAYCFR (SEQ ID NO:29)	9/9	TGF-β2	Human	P08112 (Swiss-Prot)	303-311
	fx 69 (no match)	GYNANFCAGACPYL (SEQ ID NO:30)	GYNANFCAGACPYL (SEQ ID NO:30)	14/14	TGF-β2	Human	P08112 (Swiss-Prot)	340-353
	fx 66 (1411.71)	VNSQSLSPY (SEQ ID NO:31)	VNSQSLSPY (SEQ ID NO:31)	9/9	SPP24	Bovine	Q27967 (Swiss-Prot)	42-50
25	fx 39 (1470)	KAAPKPSVP (SEQ ID NO:32)	KAAPKPSVP (SEQ ID NO:32)	8/8	Histone H1.x	Human	JC4928 (PIR)	199-206
29								

fx = fraction number (molecular weight of fragment, as measured by SDS-PAGE)

Page 31, lines 1-6, please amend as follows:

The same tryptic protein fragments were analyzed by mass spectrometry and the mass spectrograms are shown in Figures 23A-23O. The tabulated results are shown in ~~the~~ Table 3 ~~depicted in Figures 32A-32F~~, which provides identification information for each of the indicated bands, as identified in Figures 19 and 20. As above, assignment of band identity may be tentative based on species differences and post translational modifications.

Page 31, please insert the following Table after line 6:

TABLE 3
IDENTIFICATION OF PROTEINS BY MASS SPECTROMETRY SEQUENCING OF TRYPTIC FRAGMENTS

Band	Mass Spec. Profile	Species	Acc. No.	Mass Spec. Data	Mass Spec. Database	Mass Difference	AAs	% Coverage	Comments
1	4 peaks match with histone H1.c	Human	87668 (NCBI)	1172.97	1172.37	0.60	110-121	22	15 MS peaks match with Band 2
				1579.87	1579.71	0.16	65-79		
				1708.47	1707.89	0.58	64-79		
				2011.58	2012.32	-0.74	35-54		
2	3 peaks match with histone H1.c	Human	87668 (NCBI)	1579.76	1579.71	0.05	65-79*	16	Identification of starred peptide confirmed by sequence analysis
				1708.02	1707.89	0.13	64-79		
				2012.12	2012.32	-0.20	35-54		
3	7 peaks match with ribosome S20	Rat	R3RT20 (PIR)	1129.76	1129.40	0.36	50-59	62	15 MS peaks match with Band 1
				1156.21	1156.30	-0.09	78-83		
				1334.46	1334.62	-0.16	56-66		
				1352.13	1351.58	0.55	88-99		
				1518.04	1517.77	0.27	9-21		
				1919.02	1919.19	-0.17	5-21		
4	3 peaks match with Lysyl Oxidase RP	Human	NP002309 (Swiss-Prot)	3404.02	3404.87	-0.85	88-119	8	12 MS peaks match with Band 8
				1987.95	1988.27	-0.32	150-167		
				2410.35	2410.63	-0.28	648-669		
				2610.57	2610.10	0.47	455-478		

TABLE 3
IDENTIFICATION OF PROTEINS BY MASS SPECTROMETRY SEQUENCING OF TRYPTIC FRAGMENTS

Band	Mass Spec. Profile	Species	Acc. No.	Mass Spec. Data	Mass Spec. Database	Mass Difference	AAs	% Coverage	Comments
5	9 peaks match with BMP-3	Human	4557371 (NCBI)	1113.32	1113.31	0.01	361-368	48	% coverage calculation is relative to the mature BMP-3, 183 AAs (290-472)
				1438.53	1438.58	-0.05	346-357		
				1566.76	1566.76	0.00	345-357		
				1651.86	1651.91	-0.05	410-424		
				1794.09	1794.02	0.07	346-360		
				2268.46	2268.63	-0.17	374-392		
				2424.45	2424.81	-0.36	373-392		
				3409.15	3407.77	1.38	290-318*		
6	3 peaks match with α 2-Macroglobulin RAP	Human	P30533 (Swiss-Prot)	1002.24	1002.15	0.09	283-290	17	
				2362.58	2362.43	0.15	129-150		
				3048.51	3048.52	-0.01	257-282		
				1566.93	1566.75	0.18	346-357		
7	4 peaks match with ribosome L32	Mouse	P17932 (Swiss-Prot)	1651.88	1651.91	-0.03	41-424	15	% coverage calculation is relative to the mature BMP-3, 183 AAs (290-472)
				1033.25	1033.17	0.08	67-75		
				1093.31	1093.40	-0.09	1-10*		
				1134.72	1134.28	0.44	65-74		
				1449.78	1449.66	0.12	19-29		
	5 peaks match with BMP-3	Human	4557371 (NCBI)	1060.42	1060.20	0.22	102-111	21	% coverage calculation is relative to the mature
				1113.39	1113.31	0.08	361.368		

TABLE 3
IDENTIFICATION OF PROTEINS BY MASS SPECTROMETRY SEQUENCING OF TRYPTIC FRAGMENTS

Band	Mass Spec. Profile	Species	Acc. No.	Mass Spec. Data	Mass Spec. Database	Mass Difference	AAs	% Coverage	Comments
				1360.26	1360.58	-0.32	190-200		BMP-3, 183 AAAS (290-472)
				1652.28	1651.91	0.37	410-424		
				1793.62	1794.02	-0.40	346-360		
8	1 peak matches with Lysyl Oxidase RP	Human	NP002309 (Swiss-Prot)	2410.37	2410.63	-0.26	648-669	3	12 MS peaks match with Band 4
9	6 peaks match with BMP-3	Human	4557371 (NCBI)	1113.14	1113.31	-0.17	361-368	36	% coverage calculation is relative to the mature BMP-3, 183 AAS (290-472)
				1438.60	1438.58	0.02	346-357		
				1566.77	1566.76	0.01	345-357		
				1651.91	1651.61	0.30	410-424		
				2901.67	2901.19	0.48	41-66		
				3408.94	3407.77	1.17	290-318		
11	5 peaks match with BMP-3	Human	4557371 (NCBI)	1113.23	1113.31	-0.08	361-368	48	% coverage calculation is relative to the mature BMP-3, 183 AAS (290-472)
				1651.73	1651.91	-0.18	410-424		
				1793.58	1794.02	-0.44	346-360		
				2424.24	2424.81	-0.57	373-392		
				3408.34	3407.77	0.57	290-318		
	5 peaks match with ribosome L6	Human	Q02878 (Swiss-Prot)	1140.38	11409.23	0.15	114-122	16	
				1526.88	1526.86	0.02	141-155		
		Mouse	P47911	1059.15	1059.12	0.03	10-20		

TABLE 3
IDENTIFICATION OF PROTEINS BY MASS SPECTROMETRY SEQUENCING OF TRYPTIC FRAGMENTS

Band	Mass Spec. Profile	Species	Acc. No.	Mass Spec. Data	Mass Spec. Database	Mass Difference	AAs	% Coverage	Comments
18	4 peaks match with TGF- β 2	Human	(Swiss-Prot)	1145.36	1145.35	0.01	262-271	52	
				1386.74	1386.68	0.06	260-271		
				1101.20	1101.26	-0.06	303-311		
				1175.26	1175.42	-0.16	400-409		
				2240.37	2240.60	-0.23	312-328		
				2691.70	2691.91	-0.21	340-362		
22	5 peaks match with SPP24	Bovine	Q27967 (Swiss-Prot)	1410.93	1411.60	-0.67	42-53	30	
				1447.59	1447.65	-0.06	113-124		
				1540.64	1540.60	0.04	86-98		
				1869.10	1869.05	0.05	62-77		
				2268.47	2268.57	-0.10	33-53		
				1101.15	1101.26	-0.11	303-311		
25	5 peaks match with TGF- β 2	Human	P08112 (Swiss-Prot)	1175.13	1175.42	-0.29	400-409	63	
				2084.16	2084.42	-0.26	312-347		
				2240.25	2240.60	-0.35	312-328		
				2691.61	2691.91	-0.30	340-362		
				1411.23	1411.60	-0.37	42-53		
				1447.40	1447.65	-0.25	113-124		
25	2 peaks match with SPP24	Bovine	Q27967 (Swiss-Prot)	1208.46	1208.40	0.06	48-57	14	
				1221.71	1222.35	-0.64	107-118		
				JC4928 (PIR)					

TABLE 3
IDENTIFICATION OF PROTEINS BY MASS SPECTROMETRY SEQUENCING OF TRYPTIC FRAGMENTS

Band	Mass Spec. Profile	Species	Acc. No.	Mass Spec. Data	Mass Spec. Database	Mass Difference	AAs	% Coverage	Comments
	H1.x			1349.85	1350.52	-0.67	107-119		
				1364.57	1364.59	-0.02	48-58		
				1732.23	1732.97	-0.74	43-57		
	5 peaks match with BMP-3	Human	4557371 (NCBI)	1060.43	1060.02	0.23	102-111	31	% coverage calculation is relative to the mature BMP-3, 183 AAS (290-472)
				1438.83	1438.58	0.25	346-357		
				1566.92	1566.76	0.16	345-357		
				1651.80	1651.91	-0.11	410-424		
				3408.86	3407.77	1.09	290-318		
	4 peaks match with BMP-3	Human	4557371 (NCBI)	1113.22	1113.31	-0.09	361-368	27	% coverage calculation is relative to the mature BMP-3, 183 AAS (290-472)
				1438.70	1438.58	0.12	346-357		
				1566.86	1566.75	0.11	345-357		
				3409.04	3407.77	1.27	290-318		
29									

Page 31, lines 7-11, please amend as follows:

The identified components of BP were quantified as shown in Figures ~~33A~~ 30A and ~~33B~~ 30B. Figure ~~33B~~ 30B is a stained SDS-PAGE gel of BP and Figure ~~33A~~ 30A represents a scanning densitometer trace of the same gel. The identified proteins were labeled and quantified by measuring the area under the curve. These results are presented in ~~Figure 34~~ Table 4 as a percentage of the total peak area.

Page 31, please insert the following Table after line 11:

TABLE 4

QUANTITATION OF IDENTIFIED BP PROTEINS

Identified Protein	Percentage of Total Protein
LORP	2
BMP-3	11
BMP-3 and A2-MG	3
RL6 and BMP-3	4
Histone	3
Histone	3
Histone and BMP-3	4
BMP-3	8
RL32 and BMP-3	8
RS2D	5
SPP24 and TGF- β 2	6
Total	58%

Page 31, lines 12-20, please amend as follows:

As ~~Figure 34~~ Table 4 indicates, there are 11 major bands in the BP SDS-PAGE gel representing about 60% of the protein in BP. Further, TGF- β 1 was quantified using commercially pure TGF- β 1 as a standard, and was determined to represent less than 1% of the BP protein. The identified proteins fall roughly into three categories: the ribosomal proteins, the histones, and growth factors, including active growth factors comprising members of the TGF- β superfamily of growth factors, which includes the bone morphogenic proteins (BMPs). It is believed that the ribosomal proteins and histone proteins may be removed from the BP without loss of activity, and the specific activity is expected to increase correspondingly.